THE TREATMENT OF BONE TUMORS*

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DISCUSSION *by Arthur U. Desjardins, M. D., Rochester, Minnesota; John C. Wilson, M. D., Los Angeles; C. L. Connor, M. D., San Francisco.*

THE treatment of bone tumors until comparatively recently has been largely empirical and has consisted of a variety of procedures, both surgical and nonsurgical. Up to approximately the beginning of the twentieth century about the only therapeutic measure employed was high disarticulation. This penalty was meted out to practically all individuals with any type of bone lesion which could not be grouped under the heading of inflammatory processes because nothing was known about the pathology of these conditions and the few survivors up to this time had had the benefit of amputations. The opening of the twentieth century saw the beginning of an organized effort to study the pathology of bone tumors. Out of these scientific investigations, notably those by Bloodgood, came a more conservative attitude and a replacement of amputation in large measure, by other methods such as resection, curettement, x-ray or radium therapy, mixed toxin treatments, etc.

A further and better understanding of this field has come of recent years through the sarcoma registry, which has brought together large numbers of all kinds of bone tumors and has placed this material for study in available form before the leading pathologists and surgeons of the country. The outstanding advances from this source have been the confirmation of Doctor Bloodgood's contention that giant cell tumor is not sarcoma, the exclusion of bone cyst and osteitis fibrosa from among the true neoplasms, and the establishment of a simplified classification.

CLASSIFICATION OF BONE TUMORS ACCORDING TO ORIGIN

Not the least of the advantages gained in our recent scientific investigations have been the grouping together of all bone tumor lesions into a small group of eight main divisions (Table 1).

TABLE 1.—*Tumor Classification Based on Origin*

1. Metastatic tumors.
2. Periosteal fibrosarcoma.
3. Osteogenic tumors.
   - Benign.
     - a. Exostosis.
     - b. Osteoma.
     - c. Chondroma.
     - d. Fibroma.
   - Malignant (osteogenic sarcoma).
     - a. Anatomic types.
       - Medullary and subperiosteal.
       - Periosteal.
       - Sclerosing.
       - Telangiectatic.
     - b. Undifferentiated sarcoma.
4. Inflammatory conditions that may simulate bone tumors.
   1. Myositis ossificans.
   2. Osteoperiostitis.
      - a. Traumatic.
      - b. Syphilitic.
      - c. Infectious.
   3. Osteitis fibrosa (bone cyst).
5. Benign giant cell tumor.
6. Angioma.
   - Benign.
   - Malignant (angiosarcoma).
7. Ewing's tumor.
8. Myeloma.

One of the greatest stumbling blocks in the past has been the multiplicity of terms used and the various interpretations placed upon them. This classification puts all the malignancies under approximately four heads, namely, metastatic lesions, sarcoma arising from bone cells (osteogenic sarcoma), sarcoma arising from marrow cells, and endothelial myeloma (Ewing). It divides the benign tumors into those arising from the bone cell and the medullary lesions of unknown origin, that is, giant cell tumor and bone cyst.

All our old familiar terms, such as periosteal sarcoma, medullary sarcoma, spindle cell sarcoma, round cell sarcoma, osteochondromyxosarcoma, etc., are all grouped under osteogenic sarcoma. Perhaps we should also include here the separate headings in our present classification of periosteal fibrosarcoma, Ewing's tumor and angiosarcoma, but as yet these conditions have not been wholly reconciled with our conception of the term "osteogenic" or have not been, in some instances, definitely proved to belong among the tumors of bone. The classification is not a perfect one, but for the first time in the history of bone tumors we all talk a common language and we have a common starting point in our further studies.

CLASSIFICATION ACCORDING TO PROGNOSIS

To the average surgeon, however, the practical application of all this to his problem of treatment may be somewhat obscure. Fortunately there is a very close parallelism between the prognosis and the treatment, and since the morbidity is a known factor the following regrouping according to prognosis should simplify considerably the rules for treatment.

TABLE 2.—*Classification According to Prognosis*

1. Benign—curable.
   - (1) Osteogenic tumors.
     - a. Exostosis.
     - b. Osteoma.
     - c. Chondroma of the phalanges.
     - d. Fibroma (lipoma, fibrolipoma).
   - (2) Inflammatory conditions.
     - a. Osteoperiostitis.
     - b. Osteitis fibrosa (bone cyst).
   - (3) Giant cell tumor.
2. Malignant—incurable.
   - Osteogenic sarcoma.
   - Ewing's tumor.
   - Myeloma.
   - Angiosarcoma.
   - Metastatic tumors.
3. Borderline—hopeful.
   - Central chondromyxoma (except phalangeal).
   - Atypical sarcoma.

Under benign come all tumors that are curable by the comparatively simple surgical or nonsurgical procedures which do not cause mutilation, deformity, or permanent disability. Under malignant come those which are hopeless, that is, those which are rarely curable by any known therapeutic agent. Under borderline come those tumors which are questionably benign or hopeful and which, like the operable malignant tumors

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elsewhere in the body, are sometimes curable by wide excision with attending more or less mutilation and deformity.

TREATMENT OF VARIOUS GROUPS

Benign.—The tumors in the benign osteogenic group which fall under the headings of osteoma, exostosis, osteochondroma, chondroma, etc., should be treated by excision without destroying the supporting action of the skeleton. That is, the offending portion only is removed and no margin need be given. Perhaps one exception is the central chondroma which, in the long bones, oftentimes is not eradicable without resection, and for this reason these tumors have been placed in Group 3. In the phalanges, however, this same tumor runs true to form as a member of the benign osteogenic group in that simple curettement is sufficient.

Osteitis fibrosa (bone cyst) is a self-limiting disease. All that is required is a stimulation to healthy normal reaction or, in the case of bone cyst, the collapse of the rigid bony cavity. The treatment, therefore, is x-ray or an equivalent stimulus, surgical fracture.

Giant cell tumor, while not always self-limiting, is also curable under the influence of the proper stimulation to normal reaction. At one time it was thought necessary to curet and thoroughly destroy all the tumor tissue or, where this was impossible because of dangers of hemorrhage, resection was thought necessary. We now know that giant cell tumor is curable probably in all instances by x-ray or radium. These agents, while they may not cause any appreciable shrinkage in the size of the tumor mass, do bring about an ossification, and limit the further spread of the disease process.

Malignant.—In the malignant group the type of treatment is immaterial inasmuch as all therapeutic agents are inadequate. Possibly osteogenic sarcoma in its earliest stages is curable by wide resection, but unfortunately metastases have probably already taken place by the time the first evidence of the tumor is demonstrable by x-ray. While we must include osteogenic sarcoma and Ewing's tumor in the group of essentially incurable there are a few cases of registered tumors in each group which have lived without evidence of recurrence five years or more after the last treatment.

Among Ewing's tumors the eleven reported by Connor in 1926 still remain well (Table 3). There have been no additions to the list. These represent 20 per cent of the fifty-four cases then registered. These survivors owe their lives to no definite type of treatment inasmuch as they were all treated differently. All had benefit of some form of surgery except one. He had x-ray treatment only. One case had multiple skull, and even intracranial metastases, and has now been alive and apparently entirely well for ten years after his last x-ray treatment. Ewing's tumor, therefore, cannot be placed in the hopeful or borderline class because there must be some factor outside the therapeutic agents employed that gives the cure, and it would seem that it is simply a case of good or bad luck if the patient survives or dies.

Among the osteogenic sarcomata there are thirty-one five-year cures out of 125 registered cases which have been followed five years after the last treatment (Table 4). These have all been instances of tumors of the extremities and all have had amputation. None have had high disarticulation except one, a growth in the upper

TABLE 3.—*Cases of Ewing's Tumor Contained in the Registry of Bone Sarcoma, Living Five Years or More*

No.	Case No.	Sex	Age at Onset	Location	Treatment	Remarks	Duration of "cure," years
1	28	M.	13	Clavicle	Excision	Recurrence — x-ray treatment — cure(?)	5
2	137	F.	Young	Scapula and clavicle	Resection	Combined with x-ray treatment	6
3	185	F.	7	Tibia	Amputation	Followed by x-ray, radium and Coley's serum	10
4	246	M.	30	Humerus	Radium	Cure(?) under radium treatment alone	6
5	267	M.	8	Fibula	Amputation	Recurrence in groin and lungs—x-ray. Cure(?)	8
6	294	F.	9	Jaw	Curettement	Followed by x-ray and radium	7
7	311	M.	30	Tibia	Amputation	Followed by Coley's serum	7
8	326	M.	26	Humerus	Amputation	Followed by x-ray, radium and Coley's serum	7
9	348	M.	3	Femur	Amputation	Skull and intracranial metastases. Cured with x-ray, radium and Coley's serum	9
10	398	M.	21	Femur	Amputation	Followed by Coley's serum	19
11	515	M.	7	Scapula	Resection	Followed by x-ray	5

TABLE 4.—*Treatment Used in Registered Five-Year Cures of Osteogenic Sarcoma*

Number	Case Number	Surgeon	Exploratory	Curettage	Excision	Resection	Toxins	Lead	Radium	X-ray	Amputation	Cellular Type	Location
1	29	Hubbard	x	..	..	..	..	..	..	x	x	Fibrosarcoma	Tibia at knee
2	50	Rixford	x	..	..	..	..	..	..	..	x	Myxosarcoma	Femur at knee
3	64	Wells	x	..	x	..	..	..	..	..	x	Chondrosarcoma	Femur at knee
4	100	Bloodgood	..	..	x	..	x	..	x	..	x	Chondrosarcoma	Femur at knee
5	101	Bloodgood	x	..	..	..	..	..	..	..	x	Myeloma(?)	Femur at knee
6	102	Bloodgood	x	..	..	..	..	..	..	..	x	Mixed sarcoma	Tibia at knee
7	147	Simmons	..	..	x	..	..	..	..	..	x	Osteosarcoma	Humerus at shoulder
8	156	Ginsburg	..	..	..	..	..	..	..	x	x	Telangectatic sarcoma	Humerus—middle
9	172	Ewing	..	..	..	..	x	..	x	..	x	Chondromyxosarcoma	Femur at knee
10	176	Coley	..	..	x	..	x	..	x	x	x	Chondrosarcoma	
11	177	Coley	..	..	..	..	x	..	x	..	x	Chondro(?)sarcoma	
12	183	Coley	x	..	x	..	x	..	x	..	..	Fibro(?) sarcoma (atypical)	Tibia at ankle
13	184	Coley	..	..	..	..	x	..	x	..	x	Fibrosarcoma	Femur at knee
14	202	Jones	..	..	x	..	..	..	..	..	x	Chondrosarcoma	Tibia at ankle
15	214	Simmons	..	..	..	..	x	..	..	x	x	Fibro (sarcoma?)	Femur at knee
16	234	Dye	..	x	x	..	..	..	..	..	x	Chondrosarcoma	Ulna at elbow
17	261	Thompson	..	..	..	..	..	..	..	..	x	Mixed cell sarcoma	Femur at knee
18	408	Coley	..	..	..	..	x	..	..	..	x	Large round cell	Femur at knee
19	456	Coupal	..	..	..	..	..	..	..	..	x	Mixed cell sarcoma	Tibia at knee
20	501	Bloodgood	..	..	..	..	..	..	..	..	x		Femur at knee
21	537	Thompson	..	..	..	..	x	..	x	x	x	Spindle cell sarcoma	Femur at knee
22	586	Coley	x	..	..	..	x	..	x	x	x	Fibrosarcoma	
23	109	Bloodgood	..	..	..	x	..	..	x	..	..	Chondrosarcoma	Rib
24	115	Bloodgood	..	x	..	..	..	..	..	..	x	Large round cell sarcoma	Tibia at knee
25	296	Meyerding	..	..	..	..	..	..	..	..	x	Chondrosarcoma	Tibia at knee
26	312	Simmons	x	..	..	..	..	..	..	..	x	Chondromyxoosteo	Femur, lower end
27	344	Simmons	x	..	..	..	..	..	..	..	x	Fibro(sarcoma)?	Tibia at knee
28	498	Bloodgood	x	..	..	..	..	..	..	..	x		
29	523	Evans	x	..	..	..	..	..	x	x	..	Small, round cell	Left ilium
30	668	Fennel	..	..	x	..	..	..	x	..	..	Chondrosarcoma	Lower femur
31	867	Harris	..	..	x	..	..	..	..	..	..		Scapula

end of the humerus. The majority were in the lower end of the femur. The answer might lie in the type of cell making up the majority of the growth. In reviewing the microscopic pathology one is struck by the preponderance of chondromatous tissue, and when one looks at each case as a whole he is further struck by the fact that none of the cured cases were truly typical of any of the known forms of osteogenic sarcoma. This group of thirty-one cures, therefore, probably does not indicate the real situation and for the present we must consider the clinically typical case of osteogenic sarcoma as incurable.

Borderline.—In the borderline group has been placed central chondroma and central myxoma, excluding the central chondroma of the phalanx which is apparently always benign. Myxoma is possibly a modification of cartilage and therefore probably should be included under the heading of chondroma. If so, this should add weight in the placing of chondroma in the doubtful group, because it is a well-known fact that tumors elsewhere in the body which show a high percentage of myxomatous tissue are extremely difficult to eradicate locally, requiring very extensive margins. Furthermore it has been everybody's experience that chondroma tends to recur and that a simple shelling out or curetting out of the tumor is insufficient. These facts, together with the observation that a cell which resembles more or less closely the cartilage cell seemed to be the preponderating element in many of the thirty-one cured malignant tumors, might be taken to indicate that chondromatous tumors belong rather in the truly benign and innocent group than among the hopelessly malignant.

SUMMARY

In conclusion, most bone tumors are either malignant, inoperable, untreatable, and rapidly fatal or are curable, either without the necessity of surgery or by a nondisabling and nonmutilating operation. All these are quite typical and practically without exception can be positively diagnosed by the clinical evidence alone. On the other hand, a small minority which are atypical clinically may be curable by conservative amputations or wide resections. Exploratory operations are strongly indicated in this group, but can be limited to the clinically atypical cases. The employment of amputation as a treatment of bone tumors should become relatively rare. Furthermore x-ray treatment should be given a trial and should be looked to for a cure until it becomes evident that the growth will not be affected by this therapeutic agent or until the diagnosis becomes clear.

The outcome, therefore, of our recent advances gained in the study of bone tumors is not the saving of lives but the saving of limbs. We have not advanced in the cure of sarcoma and probably will not save any of the victims of this disease until we find a preventive which will render the human body immune or until we have found some means of diagnosing sarcoma at an earlier stage, that is, before there is x-ray evidence of the disease. What we have learned, however, is almost as important as saving lives. We have learned to allow our patients who are suffering with malignant bone disease to die whole under the comforting and pain-relieving effects of x-ray and morphin, and we have learned to carefully preserve the limbs affected with nonmalignant disease, thus saving their owners from a life of mutilation, deformity, and disability.

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DISCUSSION

ARTHUR U. DESJARDINS, M. D. (Mayo Clinic, Rochester).—Doctor Bartlett is to be complimented on his excellent presentation and analysis of the present situation with reference to bone tumors. I do not care to enter into a discussion of the classification of bone tumors, because even the best pathologists in the country have failed to come to an agreement on this question. I concur with Doctor Bartlett in his remarks concerning the treatment of benign and inflammatory bone conditions. I am not a surgeon but a radiologist, and any comments I may make must naturally be from the point of view of radiology.

In connection with giant cell tumors considerable evidence indicates that these lesions are essentially chronic inflammations which sometimes undergo malignant transformation. The general unfamiliarity with the effect of radiation on such lesions is still responsible for the amputation of many limbs, some of which might otherwise be saved. When a pure giant cell tumor is exposed to a moderate dose of roentgen or radium rays the treatment is followed within two weeks by a reaction characterized by swelling, pain, and redness, and the attending physician or surgeon, as well as the patient, may infer that irradiation has increased rather than decreased the growth of the tumor. This reaction is only temporary, however, and subsides in a week or ten days. It is followed by slow but gradual repair, including deposition of new bone, and in the course of six to twelve months the lesion may have been completely replaced by solid new bone. Unfortunately, it is sometimes difficult to be certain whether such a tumor is entirely benign or whether it may contain malignant elements, and this throws on the attending physician or surgeon, as well as on the radiologist who may be treating the patient, a grave responsibility. If any such doubt exists it must at all costs be removed and the treatment must rest on this point. Also the economic situation of the patient must be considered.

Among the true bone tumors some are relatively radiosensitive and others relatively resistant. Perhaps the most sensitive malignant tumor of bone is the endothelial myeloma of Ewing, which can often be made to disappear, sometimes permanently, but which may later exhibit metastasis in spite of the disappearance of the primary tumor. The chondrosarcoma comes next in radiosensitiveness. The fibrosarcoma is comparatively resistant. Some tumors of this kind retrogress to some extent under irradiation, but they seldom disappear completely, and even if they do, nearly always recur. Tumors containing any considerable degree of myxomatous tissue usually exhibit a high degree of resistance and irradiation has little effect on growths of this kind.

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JOHN C. WILSON, M. D. (1136 West Sixth Street, Los Angeles).—Doctor Bartlett has well summarized the gravity of the malignant bone tumor, as contrasted with the very gratifying results which may be obtained in the nonmalignant group, by means of nondeforming therapeutic procedures. Unfortunately, the early diagnosis of bone tumors is beset in many cases with formidable difficulties. The roentgenograms are sometimes characteristic and pathognomonic, but all too frequently the roentgenologist is unable to tell us with absolute certainty the nature of the presenting lesion. We have seen a classical x-ray picture of osteogenic sarcoma produced by tertiary syphilis.

Of all the malignant tumors Ewing's endothelioma is perhaps the most protean in its manifestations. It is often clinically indistinguishable from chronic osteomyelitis and presents a very similar x-ray appearance. Recently we have seen a Ewing's tumor which gave the characteristic x-ray picture of Brodie's abscess. When faced by such uncertainties as these the surgeon is obliged to perform an exploratory operation, remove a tissue section, and turn to the pathologist for further information; but even here we encounter a difference of opinion which is disconcerting when one must decide whether or not to amputate.

One addition to Doctor Bartlett's borderline group is suggested: the angiosarcoma of relatively low malignancy apparently offers a fairly good chance of cure by early amputation. The benign angioma if it involves any considerable amount of bone also belongs in this group because of the fact that a rather extensive resection of the bone may be required.

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C. L. CONNOR, M. D. (University of California Hospital, San Francisco).—I believe Doctor Bartlett has given, perhaps for the first time in the history of bone tumors, a clinical classification which is practical and useful. I should not wish to think, however, that all of the groups which he calls incurable are always and quite definitely incurable. I should, as Doctor Wilson has done, remove this peculiar tumor which we now call angiosarcoma from the definitely incurable group and say that, provided proper surgical treatment is initiated, it may be curable, that is to say, removed. I should also ask that Ewing's tumor, or at least a certain percentage of them, be placed in the borderline group. We know that some arise very suddenly, metastasize very early and produce death in an extremely short time. There are others, however, which may be removed in time. I do not entirely agree with Ewing that this tumor is multiple from the beginning and that, therefore, amputation is of no value. I should advise amputation or excision in all of these cases and should expect that in a small percentage a permanent cure could be effected.

DOCTOR BARTLETT (Closing).—The main point which I wished to bring out was that of surgical conservatism, that is, the avoidance of amputation if possible, and resection rather than high disarticulation. No case should be submitted to amputation without definite proof that the condition is malignant and, contrary to the principles of surgery in malignant disease elsewhere in the body, it is well to take time for careful study before deciding on the type of treatment to be employed. Having decided upon amputation one should resect rather than disarticulate, because, with rare exceptions, any bone malignancy which is not curable by resection with a moderate margin, is not curable by the highest disarticulation. During the period of study, x-ray should be employed because a moderate amount of x-ray can do no harm in benign disease and it might bring some benefit in malignant disease.

I must agree that angiosarcoma is sometimes curable by amputation during the early stages of the disease. The picture in the x-ray is fairly typical, but not until the process is quite advanced. It would be caught, therefore, in its early stages in the atypical group and would probably have the benefit of an exploratory operation.

DIFFERENTIATION BETWEEN YAWS AND SYPHILIS*

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DISCUSSION *by Fred R. Fairchild, M. D., Woodland; Alfred C. Reed, M. D., San Francisco.*

YAWS (framboesia, paranghi, puru, gueos) is a disease of the tropics and especially of the South Sea Islands and western Pacific, including the Dutch Indies and Malaya. I encountered it first in 1912, 1913 and 1914 while in the British Colonial service as senior medical officer and deputy commissioner of the western Pacific. Later, after the war, I had to deal with it in the Malay states. In the western Pacific my government statistics showed that it occurred in the ratio of one to three of the population.

Until comparatively recent times this disease was described only in books on skin diseases, and its general character was unrecognized. Inasmuch as the interchange of trade and passengers between the islands of the Pacific Ocean and this coast is on the rapid increase, it is necessary that the disease should be easily recognized else it will gain a foothold and become endemic in the subtropical parts of this country.

STAGES

The lesions of yaws divide themselves into three stages—primary, secondary, and tertiary. However, it should be stated that there are authorities who still deny the tertiary stage. This is probably due to the superficial similarity between the late secondary and tertiary manifestation of yaws and those of syphilis. In a community harboring both diseases the tertiary lesions of yaws would be ascribed to syphilis owing to the nonrecognition of the disease.

BACTERIOLOGY

The microörganism causing yaws is a slender treponema called *Treponema pertenuis* by Castellani, and is indistinguishable from the *Treponema pallida* of syphilis. It is constant in the primary lesion and in the unbroken secondary papule. It is found, also, in the lymph glands, spleen, and bone marrow. It is not demonstrable in the blood, but that the blood can be used as an infective agent is proved by monkeys developing typical lesions containing the treponema when injected with blood from an infected person.

INOCULATION IN MAN

Paulet, in 1848, inoculated negroes with the secretion from yaws lesions and found the incubation period to be twelve to twenty days. The primary or "mother" yaw mostly appeared at the site of inoculation. Charlouis, in 1881, inoculated Chinese in the same manner and with similar results. He later inoculated a Chinaman suffering from yaws, with syphilis. A typical primary sore developed. I have had out-patients in my island hospital at Tarawa, Gilbert Islands, suffering from yaws develop a chancre in the days before salvarsan was used as a treatment for yaws, this proving the separate identity of the two diseases.

HISTOPATHOLOGY

The microscopic pathology of yaws has been studied by Unna, McLeod, Jeanselme, Plehn, Schuffner, Marshall, Shannon, Sieburt, Craig, Lehn, and many others. The outstanding feature is that yaws affects the epithelium rather than the cutis, the *Treponema pertenuis* being found in the epithelial layer. In the papules the surface epithelium is greatly increased in thickness and numerous elongated down-growths seen. The corium is the seat of marked edema with a diffuse cellular infiltration of polymorphonuclear, large and small mononuclear, eosinophil, and plasma cells. In the older nodules the plasma cells are present in enormous numbers. There is an absence of the perivascular mononuclear infiltration and endothelial proliferation so characteristic of syphilis.

PRIMARY STAGE

The primary stage is manifested by a soft papule, soon becoming a painful ulcer, in which the *Treponema pertenuis* can be found. The papule is usually extragenital and is not indurated. Its site depends upon the habits of the people. In the Pacific Islands it generally occurs on the lower limbs about the ankle. The natives fish on coral reefs by night and suffer many abrasions on feet and ankles, any of which provide a point of entry. The glands of the groin usually enlarge, but do not suppurate. In the Cingalese and southern Indian women, owing to their habit of carrying children astride the hip, the primary sore is frequently found there, while the children show the lesions in the crotch and about the external genitals. This primary sore, or "mother" yaw, often persists late into the secondary period and when healed can cause deformity from cicatrices.

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